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USPT	5420136.pn.	1	<a href="#">L1</a>

L12 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 1  
 ACCESSION NUMBER: 2000:184237 CAPLUS  
 TITLE: Protection from cytotoxic effects induced by the nitrogen mustard mechlorethamine on human bronchial epithelial cells in vitro  
 AUTHOR(S): Rappeneau, Stephane; Baeza-Squiban, Armelle; Jeulin, Claudette; Marano, Francelyne  
 CORPORATE SOURCE: Laboratoire de Cytophysiologie et Toxicologie Cellulaire, Universite Paris VII-Denis Diderot, Paris, 75251, Fr.  
 SOURCE: Toxicol. Sci. (2000), 54(1), 212-221  
 CODEN: TOSCF2; ISSN: 1096-6080  
 PUBLISHER: Oxford University Press  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The present study was undertaken to find potent mols. against the toxicity of nitrogen mustard mechlorethamine (HN2) on respiratory epithelial cells, using a human bronchial epithelial cell line (16HBE14o-) as an in vitro model. The compds. examd. included **inhibitors** of poly(ADP-ribose) polymerase (**PARP**), sulfhydryl-group donors as nucleophiles, and iron chelators and **inhibitors** of lipid peroxidn. as antioxidants. Their effectiveness was detd. upon observance of metabolic dysfunction induced by HN2 following a 4-h exposure, using (3-(4,5-dimethylthiazole-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) redn. and ATP-level assays as indicators. Moreover, the fluorescent probe, monobromobimane (mBBR), and 2',7'-dichlorofluorescein-diacetate (H2DCF-DA) were used to assess intracellular sulfhydryl and peroxide level modifications by flow cytometry, resp., following a 3-h exposure. At last, cell death was assessed by flow cytometry using the propidium iodide (PI)-dye-exclusion assay following 24-h exposure. **PARP inhibitors** (niacinamide, 3-aminobenzamide, 6(5H)-phenanthridinone), and two sulfhydryl-group donors (N-acetylcysteine, WR-1065) were found to be effective in preventing HN2-induced metabolic dysfunction when added in immediate or delayed treatment with HN2. Only N-acetylcysteine, however, was found to prevent cell death induced by HN2, though it must be present at the time of the HN2 challenge. Flow cytometric measurements of intracellular sulfhydryl levels strongly suggested that N-acetylcysteine and WR-1065 are preventive in alkylation of cellular compds., mainly by direct extracellular interaction with HN2. **PARP inhibitors** prevent secondary deleterious effects induced by HN2, considering metab. dysfunction as the endpoint. Elsewhere, the oxidative stress appears to be a side effect in HN2 toxicity only upon considering the inefficiency of several antioxidants.

L12 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2000 ACS  
 ACCESSION NUMBER: 1999:184260 CAPLUS  
 DOCUMENT NUMBER: 130:209323  
 TITLE: Preparation of **PARP inhibitors**  
 INVENTOR(S): Jackson, Paul F.; Li, Jia-He; Maclin, Keith M.; Zhang,

PATENT ASSIGNEE(S): Jie Guilford Pharmaceuticals Inc., USA  
 SOURCE: PCT Int. Appl., 107 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 7  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9911649	A2	19990311	WO 1998-US18185	19980902
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9893748	A1	19990322	AU 1998-93748	19980902
PRIORITY APPLN. INFO.:			US 1997-922520	19970903
			US 1997-922548	19970903
			US 1998-79512	19980515
			US 1998-145176	19980901
			WO 1998-US18185	19980902

AB **PARP inhibitors** were prepd. and tested for their  
 activity. E.g., 8-(aminocarbonyl)-4-quinolinecarboxylic acid was prepd.

L12 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1999:184255 CAPLUS

DOCUMENT NUMBER: 130:218330

TITLE: Di-N-heterocyclic compounds, therapeutic methods, and  
 compositions for **inhibiting** poly(ADP-ribose)  
 polymerase (**PARP**) activity

INVENTOR(S): Jackson, Paul F.; Maclin, Keith M.; Zhang, Jie

PATENT ASSIGNEE(S): Guilford Pharmaceuticals Inc., USA

SOURCE: PCT Int. Appl., 130 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

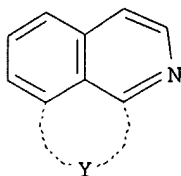
FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9911644	A1	19990311	WO 1998-US18188	19980902
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9892981	A1	19990322	AU 1998-92981	19980902
PRIORITY APPLN. INFO.:			US 1997-922520	19970903
			US 1998-79511	19980515
			US 1998-145185	19980901
			WO 1998-US18188	19980902

OTHER SOURCE(S): MARPAT 130:218330

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AB Compds. I [Y = atoms necessary to form fused 5- to 6-membered, arom. or non-arom., (un)substituted heterocyclic ring contg. .gtoreq.1 N in a 1,3-relationship with N depicted] or a pharmaceutically acceptable salt, hydrate, ester, solvate, prodrug, metabolite, stereoisomer, or mixt. thereof, are disclosed for **inhibiting PARP** activity.

L12 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1999:184241 CAPLUS

DOCUMENT NUMBER: 130:218329

TITLE: Alkoxy-substituted heterocyclic compounds, therapeutic

methods, and compositions for **inhibiting** poly(ADP-ribose) polymerase (**PARP**) activity

INVENTOR(S): Jackson, Paul F.; Maclin, Keith M.; Zhang, Jie

PATENT ASSIGNEE(S): Guilford Pharmaceuticals Inc., USA

SOURCE: PCT Int. Appl., 151 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

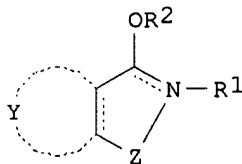
FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9911628	A1	19990311	WO 1998-US18226	19980902
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 9892991	A1	19990322	AU 1998-92991	19980902
PRIORITY APPLN. INFO.:			US 1997-922520	19970903
			US 1998-79508	19980515
			US 1998-145166	19980901
			WO 1998-US18226	19980902

OTHER SOURCE(S): MARPAT 130:218329

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AB The invention discloses **PARP-inhibiting** alkoxy-substituted heterocyclic compds., compns., therapeutic methods of use, and processes of making these compds. The compds. are I [R1 (when present) = H, lower alkyl; R2 = lower alkyl, aryl, aralkyl, lower

alkanoyl, (CH<sub>2</sub>)<sub>n</sub>(CHOH)<sub>y</sub>(CH<sub>2</sub>)<sub>m</sub>A (n = 1-4; y = 0, 1; m = 0-5; A = cycloalkyl, cycloalkenyl, lower alkanoyl, aryl, aralkyl, NH<sub>2</sub>, etc.); Y = atoms necessary to form fused 5- to 6-membered ring that is arom. or nonarom. and carbocyclic or heterocyclic; Z = (i) CHR<sub>2</sub>CHR<sub>3</sub> (R<sub>2</sub>, R<sub>3</sub> = H, alkyl, aryl, aralkyl); (ii) R<sub>6</sub>C=CR<sub>3</sub> (R<sub>6</sub>, R<sub>3</sub> = H, lower alkyl, aryl, etc., or R<sub>6</sub> and R<sub>3</sub> taken together form fused 5- to 6-membered ring that is arom. or nonarom. and carbocyclic or heterocyclic); (iii) R<sub>2</sub>C=N; (i.v.) CR<sub>2</sub>(OH)NR<sub>7</sub>; (v) C(O)NR<sub>7</sub>; R<sub>7</sub> = H, lower alkyl] or a pharmaceutically acceptable salt, hydrate, ester, solvate, prodrug, metabolite, stereoisomer, or mixts. thereof.

L12 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1999:184237 CAPLUS

DOCUMENT NUMBER: 130:218328

TITLE: Oxo-substituted heterocyclic compounds, therapeutic methods, and compositions for **inhibiting** poly(ADP-ribose) polymerase (**PARP**) activity

INVENTOR(S): Li, Jia-He; Tays, Kevin L.; Zhang, Jie

PATENT ASSIGNEE(S): Guilford Pharmaceuticals Inc., USA

SOURCE: PCT Int. Appl., 152 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

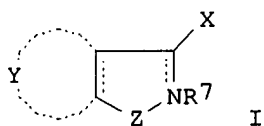
FAMILY ACC. NUM. COUNT: 7

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9911624	A1	19990311	WO 1998-US18195	19980902
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 9892986	A1	19990322	AU 1998-92986	19980902
PRIORITY APPLN. INFO.:			US 1997-922520	19970903
			US 1998-79509	19980515
			US 1998-145180	19980901
			WO 1998-US18195	19980902

OTHER SOURCE(S): MARPAT 130:218328

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AB **PARP-inhibiting** oxo-substituted heterocyclic compds., compns. contg. them, therapeutic methods of using them, and processes for making them are disclosed. The compds., contg. at least one ring nitrogen, are I [X = double-bonded O, OH; R<sub>7</sub> (when present) = H, lower alkyl; Y = atoms necessary to form fused mono-, bi- or tricyclic, carbocyclic or heterocyclic ring, wherein each individual ring has 5-6 ring member atoms; Z = (i) CHR<sub>2</sub>CHR<sub>3</sub> (R<sub>2</sub>, R<sub>3</sub> = H, alkyl, aryl, aralkyl); (ii) R<sub>6</sub>C=CR<sub>3</sub> (R<sub>3</sub>, R<sub>6</sub> = H, lower alkyl, aryl, aralkyl, halo, NO<sub>2</sub>, COOR<sub>7</sub>, NR<sub>7</sub>R<sub>8</sub> (R<sub>8</sub> = H, C<sub>1</sub>-C<sub>9</sub> alkyl), or R<sub>6</sub> and R<sub>3</sub> taken together form fused arom. ring, wherein each individual ring has 5-6 ring members); (iii) R<sub>2</sub>C=N;

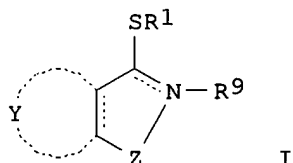
(i.v.) CR2(OH)NR7; (v) C(O)NR7] or a pharmaceutically acceptable base or acid addn. salt, hydrate, ester, solvate, prodrug, metabolite, stereoisomer or mixt. thereof.

L12 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1999:184236 CAPLUS  
DOCUMENT NUMBER: 130:218327  
TITLE: Thioalkyl-substituted heterocyclic compounds,  
therapeutic methods, and compositions for  
inhibiting poly(ADP-ribose) polymerase (  
PARP) activity  
INVENTOR(S): Jackson, Paul F.; Maclin, Keith M.; Zhang, Jie  
PATENT ASSIGNEE(S): Guilford Pharmaceuticals Inc., USA  
SOURCE: PCT Int. Appl., 130 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 7  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9911623	A1	19990311	WO 1998-US18184	19980902
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9892978	A1	19990322	AU 1998-92978	19980902
PRIORITY APPLN. INFO.:			US 1997-922520	19970903
			US 1998-79513	19980515
			US 1998-145179	19980901
			WO 1998-US18184	19980902

OTHER SOURCE(S): MARPAT 130:218327  
GI

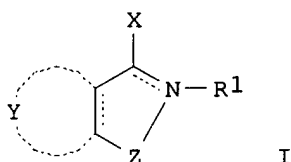


AB Compds. I [R1 = lower alkyl, lower alkenyl, lower alkynyl; R9 (when present) = H, lower alkyl; Y = atoms necessary to form fused 5- to 6-membered ring that is arom. or nonarom. and carbocyclic or heterocyclic;  
Z = (i) CHR2CHR3 (R2, R3 = H, alkyl, aryl, aralkyl); (ii) R6C=CR3 (R6, R3 = H, lower alkyl, aryl, aralkyl, Cl, Br, NR7R8 (R7, R8 = H, lower alkyl) or R6 and R3 taken together form fused 5- to 6-membered ring that is arom. or nonarom. and carbocyclic or heterocyclic); (iii) R2C=N; (i.v.) CR2(OH)NR7; (v) C(O)NR7], or a pharmaceutically acceptable salt, hydrate, ester, solvate, prodrug, metabolite, stereoisomer, or mixts. thereof, are disclosed, as are therapeutic methods and compns. for inhibiting poly(ADP-ribose) polymerase (PARP) activity.

L12 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2000 ACS  
ACCESSION NUMBER: 1999:184235 CAPLUS

DOCUMENT NUMBER: 130:218326  
 TITLE: Amino-substituted heterocyclic compounds, therapeutic methods, and compositions for **inhibiting** poly(ADP-ribose) polymerase (**PARP**) activity  
 INVENTOR(S): Jackson, Paul F.; Maclin, Keith M.; Zhang, Jie  
 PATENT ASSIGNEE(S): Guilford Pharmaceuticals Inc., USA  
 SOURCE: PCT Int. Appl., 137 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 7  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9911622	A1	19990311	WO 1998-US18187	19980902
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9892980	A1	19990322	AU 1998-92980	19980902
PRIORITY APPLN. INFO.:			US 1997-922520	19970903
			US 1998-79507	19980515
			US 1998-145177	19980901
			WO 1998-US18187	19980902
OTHER SOURCE(S):			MARPAT 130:218326	
GI				



AB Compds. I [R1 (when present) = H, lower alkyl; X = NR4R5 (R4, R5 = H, lower alkyl, aralkyl, aryl, etc.); Y = atoms necessary to form fused 5- to 6-membered ring that is arom. or nonarom. and carbocyclic or heterocyclic;  
 Z = (i) CHR2CHR3 (R2, R3 = H, alkyl, aryl, aralkyl); (ii) R6C=CR3 (R6, R3 = H, lower alkyl, aryl, aralkyl, chlorine, bromine, NR7R8 (R7, R8 = H, lower alkyl), or R6 and R3 taken together form fused 5- to 6-membered ring that is arom. or nonarom. and carbocyclic or heterocyclic); (iii) R2C=N; (i.v.) CR2(OH)NR7; (v) C(O)NR7], or a pharmaceutically acceptable salt, hydrate, ester, solvate, prodrug, metabolite, stereoisomer, or mixt. thereof, pharmaceutical compns. contg. them, therapeutic methods for using them, and processes for making them are disclosed.

L12 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 2  
 ACCESSION NUMBER: 2000:264150 CAPLUS  
 TITLE: Effects of **PARP** inhibition on drug and FAS-induced apoptosis in leukaemic cells  
 AUTHOR(S): Richardson, Deborah S.; Allen, Paul D.; Kelsey,

Stephen M.; Newland, Adrian C.  
CORPORATE SOURCE: Department of Haematology, St. Bartholomew's and  
Royal London School of Medicine, UK  
SOURCE: Adv. Exp. Med. Biol. (1999), 457 (Drug Resistance in  
Leukemia and Lymphoma III), 267-279  
CODEN: AEMBAP; ISSN: 0065-2598  
PUBLISHER: Kluwer Academic/Plenum Publishers  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Poly (ADP-ribose) polymerase (**PARP**) is activated following  
binding to DNA strand breaks and is cleaved in cells undergoing  
apoptosis. Work predominantly in murine systems has suggested that **inhibitors**  
of **PARP** might potentiate the effects of chemotherapeutic agents  
and be used as adjuncts to cancer therapy. Therefore, we studied the  
role of **PARP** in drug-induced apoptosis in HL-60, myeloid leukemia  
cells and found that pre-treatment with 3-aminobenzamide (3AB) or 6(5H)-  
**phenanthridinone**, **inhibitors** of **PARP**, resulted  
in resistance to, rather than potentiation of apoptotic death induced by  
DNA-damaging agents, idarubicin, etoposide and fludarabine, as detd. by  
flow cytometry, following propidium iodide staining. 3AB treated  
CEM/VLB100, mdr-expressing human lymphoblastic leukemia cells were also  
found to be more resistant to idarubicin compared to cells treated with  
idarubicin alone, however, apoptosis was not reduced in parental CCRF-CEM  
cells under the same conditions. Similar results were obtained using  
agents with primary modes of action which do not involve DNA damage,  
vinblastine and a fas-ligating antibody (CH11). The precise role of  
**PARP** has yet to be defined but might involve effects on cell cycle  
progression. We conclude that **PARP** activation appears to be  
involved in apoptosis in certain leukemic cell lines and that these  
effects are independent of lineage or p-glycoprotein. Constitutive  
failure to activate **PARP** might be responsible for conferring  
resistance to apoptosis.

L12 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 3  
ACCESSION NUMBER: 1998:61266 CAPLUS  
DOCUMENT NUMBER: 128:165850  
TITLE: Peroxynitrite and hydrogen peroxide induced cell  
death in the NSC34 neuroblastoma .times. spinal cord cell  
line: role of poly(ADP-ribose) polymerase  
AUTHOR(S): Cookson, Mark R.; Ince, Paul G.; Shaw, Pamela J.  
CORPORATE SOURCE: MRC Neurochemical Pathology Unit, Newcastle General  
Hospital, Newcastle upon Tyne, NE4 6BE, UK  
SOURCE: J. Neurochem. (1998), 70(2), 501-508  
CODEN: JONRA9; ISSN: 0022-3042  
PUBLISHER: Lippincott-Raven Publishers  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB The reaction of superoxide and nitric oxide results in the formation of  
peroxynitrite, a long lived and highly reactive oxidant species. It has  
been suggested that the formation of peroxynitrite in vivo may contribute  
to cell death in some neurol. conditions. We have examd. the effect of  
peroxynitrite on cell death in the NSC34 spinal cord cell line. A brief  
(30 min) exposure to either peroxynitrite or hydrogen peroxide caused  
delayed cell death with an EC50 for both of .apprx.1 mM. Cell death was  
prevented by the RNA synthesis **inhibitor** actinomycin D and  
included DNA damage as an early event. We sought to clarify the  
potential role of the DNA binding enzyme poly(ADP-ribose) polymerase (**PARP**  
) in cell death in these cells. Several **PARP inhibitors**  
[benzamide, 3-aminobenzamide, nicotinamide, and 6(5H)-  
**phenanthridinone**] prevented cell death, but the inactive analog



benzoic acid did not. However, there was no evidence of cleavage of **PARP**, which occurs in apoptosis via the activation of the caspase CPP32. Therefore, we suggest that **PARP** contributes to neuronal injury as an early event, probably by lethal NAD depletion, without any requirement for proteolytic cleavage.

L12 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 4  
ACCESSION NUMBER: 1998:15201 CAPLUS  
DOCUMENT NUMBER: 128:138099  
TITLE: Effect of 6(5H)-**phenanthridinone**, a poly  
(ADP-ribose)polymerase **inhibitor**, and  
ionizing radiation on the growth of cultured lymphoma  
cells  
AUTHOR(S): Weltin, D.; Holl, V.; Hyun, J. W.; Dufour, P.;  
Marchal, P.; Bischoff, P.  
CORPORATE SOURCE: Laboratoire de Cancerologie Experimentale et de  
Radiobiologie, Institut d'Hematologie et  
d'Immunologie, Faculte de Medecine, Strasbourg,  
F-67085, Fr.  
SOURCE: Int. J. Radiat. Biol. (1997), 72(6), 685-692  
CODEN: IJRBE7; ISSN: 0955-3002  
PUBLISHER: Taylor & Francis Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB A new potent poly(ADP-ribose)polymerase (**PARP**) **inhibitor**  
, 6(5H)-**phenanthridinone** (Phen), at 100 .mu.M, **inhibited**  
>90% of the **PARP** activity in control and irradiated (60Co  
panoramic source) RDM4 murine lymphoma cells. Phen sharply increased the  
radiation-induced **inhibition** of cell proliferation, as assessed  
using the Alamar Blue fluorometric assay. At 2.5 Gy, the relative cell  
no. of Phen-treated cells was 60% below control levels and the G2M arrest  
was significantly reinforced by the addn. of Phen. Phen significantly  
increased the amt. of DNA fragmentation as revealed by the DNA migration  
pattern in agarose gel electrophoresis. Comparable results were obtained  
with 3-aminobenzamide, another **PARP inhibitor**, but at  
concns. 200-fold higher. These results indicate the potential interest  
of  
Phen as a valuable pharmacol. probe for investigating the role of  
**PARP** in cellular responses to radiation and for use as an adjuvant  
in radiotherapy.

L12 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 5  
ACCESSION NUMBER: 1996:255377 CAPLUS  
DOCUMENT NUMBER: 124:332107  
TITLE: N-acetylcysteine protects lymphocytes from nitrogen  
mustard-induced apoptosis  
AUTHOR(S): Weltin, D.; Aupeix, K.; Iltis, C.; Cuillerot, J. M.;  
Dufour, P.; Marchal, J.; Bischoff, P.  
CORPORATE SOURCE: Inst. Hematol. Immunol., Strasbourg, F-67091, Fr.  
SOURCE: Biochem. Pharmacol. (1996), 51(9), 1123-9  
CODEN: BCPCA6; ISSN: 0006-2952  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB The ability of the antioxidant N-acetylcysteine to prevent apoptosis  
induced in lymphocytes by nitrogen mustard (HN2) was investigated. HN2  
caused a concn.-dependent induction of apoptosis on C3H murine spleen  
cells, as identified by two criteria: morphol. features revealed by  
microscopical observations and DNA fragmentation visualized by the  
characteristic "ladder" pattern obsd. upon agarose gel electrophoresis,  
as  
well as by hypodiploid DNA-contg. cells revealed by the flow cytometric  
anal. of propidium iodide labeled cells. The antioxidant  
N-acetylcysteine  
(NAC) was found to markedly reduce the occurrence of HN2-induced  
apoptosis

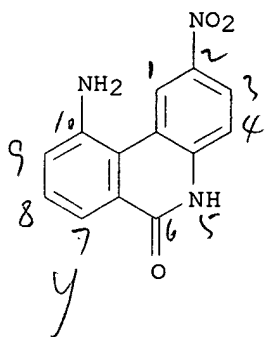
in these cells. This protective effect was still obtained when NAC was added 30 min after HN2. In contrast, the pretreatment of spleen cells with this antioxidant did not provide any significant protection. The authors also showed that lymphocytes protected by NAC are still able to respond to a mitogenic stimulation. To gain some insight into the mechanisms underlying the cytoprotective action of NAC against HN2, the authors tested whether or not poly(ADP-ribose) polymerase (**PARP**, EC 2.4.2.30), a nuclear enzyme that participates in the triggering of apoptosis induced by alkylating agents, is involved. The authors report that 6(5H)-**phenanthridinone**, a potent **PARP** inhibitor, did not affect the ability of NAC to prevent HN2-induced apoptosis under the authors exptl. conditions. Thus, the exact mechanism by which NAC protects lymphocytes from HN2 cytotoxicity has yet to be detd.

L12 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 6  
 ACCESSION NUMBER: 1995:614338 CAPLUS  
 DOCUMENT NUMBER: 123:505  
 TITLE: Immunosuppressive activities of 6(5H)-**phenanthridinone**, a new poly(ADP-ribose)polymerase inhibitor  
 AUTHOR(S): Weltin, D.; Picard, V.; Aupeix, K.; Varin, M.; Oth, D.; Marchal, J.; Dufour, P.; Bischoff, P.  
 CORPORATE SOURCE: Ins. Hematologie Immunologie, Place Hopital, Strasbourg, F-67091, Fr.  
 SOURCE: Int. J. Immunopharmacol. (1995), 17(4), 265-71  
 CODEN: IJIMDS; ISSN: 0192-0561  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB 6(5H)-**phenanthridinone**, a recently identified poly(ADP-ribose)polymerase (**PARP**) inhibitor, is able, at micromolar concns., to inhibit Con A-induced lymphocyte proliferation and to potentiate the effect of gamma radiation upon murine spleen cells. When added at the onset of a mixed lymphocyte culture, this compd. strongly depresses the induction of primary allogeneic (anti-H2k) cytotoxic T-lymphocytes (CTLs). Lymphokine-activated killer (LAK) induction was also found to be impaired by the **PARP** inhibitor. Taken together, these results clearly indicate that **PARP** plays a key-role in immune reactions involving cytotoxicity and that 6(5H)-**phenanthridinone** could be considered as a potent immunomodulator.

L12 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 7  
 ACCESSION NUMBER: 1995:472055 CAPLUS  
 DOCUMENT NUMBER: 122:230262  
 TITLE: Effect of 6(5H)-**phenanthridinone**, an inhibitor of poly(ADP-ribose) polymerase, on cultured tumor cells  
 AUTHOR(S): Weltin, Denis; Marchal, Jean; Dufour, Patrick; Potworowski, Edouard; Oth, Daniel; Bischoff, Pierre  
 CORPORATE SOURCE: Institut d'Hematologie et d'Immunologie, Place de l'Hopital, Strasbourg, F-67091, Fr.  
 SOURCE: Oncol. Res. (1994), 6(9), 399-403  
 CODEN: ONREE8; ISSN: 0965-0407  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB By catalyzing posttranslational modifications of nuclear proteins, poly(ADP-ribose) polymerase (**PARP**) controls their functions and therefore constitutes an enzyme of crucial importance in tumor development. In this study, we have investigated the action of 6(5H)-**phenanthridinone**, an isoquinoline deriv. and one of the most potent **PARP** inhibitors described so far, on RDM4 murine lymphoma cells in culture. We also examd. whether this compd. could act synergistically with an antineoplastic drug in tumor-cell

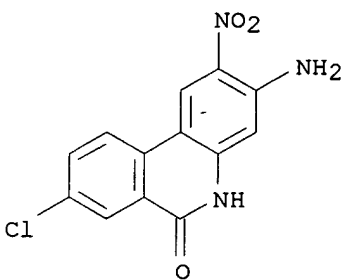
destruction. Our results demonstrate that a marked **inhibition** of **PARP** activity can be obtained in whole cells after a short incubation, and that this compd., when assocd. with an alkylating agent, chloromethine, leads to a marked drop in the RDM4 proliferation, indicative of a synergy between the two compds.

L4 ANSWER 1 OF 5 REGISTRY COPYRIGHT 2000 ACS  
RN 221081-52-3 REGISTRY  
CN 6(5H)-Phenanthridinone, 10-amino-2-nitro- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C13 H9 N3 O3  
SR CA  
LC STN Files: CA, CAPLUS, TOXLIT



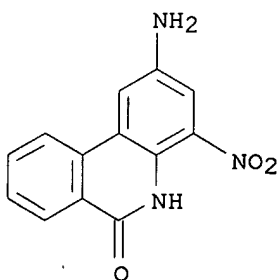
1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L4 ANSWER 2 OF 5 REGISTRY COPYRIGHT 2000 ACS  
 RN 26689-70-3 REGISTRY  
 CN **6(5H)-Phenanthridinone, 3-amino-8-chloro-2-nitro- (8CI)** (CA INDEX NAME)  
 FS 3D CONCORD  
 MF C13 H8 Cl N3 O3  
 LC STN Files: BEILSTEIN\*, CA, CAPLUS  
 (\*File contains numerically searchable property data)



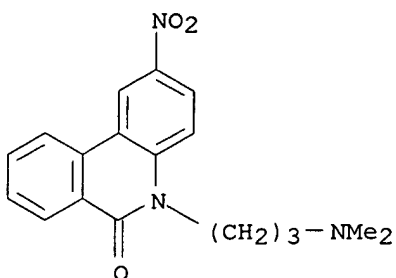
1 REFERENCES IN FILE CA (1967 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L4 ANSWER 3 OF 5 REGISTRY COPYRIGHT 2000 ACS  
 RN 23818-41-9 REGISTRY  
 CN **6(5H)-Phenanthridinone, 2-amino-4-nitro- (8CI, 9CI)** (CA INDEX NAME)  
 FS 3D CONCORD  
 MF C13 H9 N3 O3  
 LC STN Files: BEILSTEIN\*, CA, CAPLUS, CASREACT, TOXLIT  
 (\*File contains numerically searchable property data)



3 REFERENCES IN FILE CA (1967 TO DATE)  
 3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

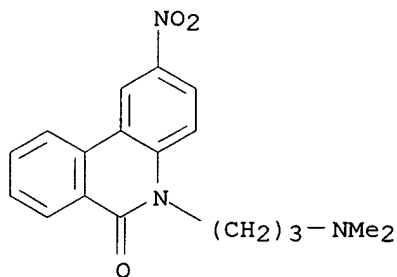
L4 ANSWER 4 OF 5 REGISTRY COPYRIGHT 2000 ACS  
 RN 22463-54-3 REGISTRY  
 CN **6(5H)-Phenanthridinone, 5-[3-(dimethylamino)propyl]-2-nitro-, monohydrochloride (8CI, 9CI)** (CA INDEX NAME)  
 MF C18 H19 N3 O3 . Cl H  
 LC STN Files: CA, CAPLUS  
 CRN (22463-53-2)



● HCl

2 REFERENCES IN FILE CA (1967 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L4 ANSWER 5 OF 5 REGISTRY COPYRIGHT 2000 ACS  
RN 22463-53-2 REGISTRY  
CN **6(5H)-Phenanthridinone, 5-[3-(dimethylamino)propyl]-2-nitro- (8CI, 9CI)** (CA INDEX NAME)  
FS 3D CONCORD  
MF C18 H19 N3 O3  
CI COM  
LC STN Files: BEILSTEIN\*, CA, CAPLUS  
(\*File contains numerically searchable property data)



2 REFERENCES IN FILE CA (1967 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)